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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,469	06/22/2001	Christine D. Krempl	NIH-013/E-225-00/1	6953

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EXAMINER
BROWN, STACY S

ART UNIT	PAPER NUMBER
1648	14

DATE MAILED: 03/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,469	KREMPL ET AL.	
	Examiner	Art Unit	
	Stacy S Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-207* is/are pending in the application.

4a) Of the above claim(s) *68-95,100-108 and 113-207* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-67,96-99 and 109-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-67, 96-99 and 109-114 is acknowledged and entered. Claims 113 and 114 were improperly included in Group I. Claims 113 and 114 belong in Group II, being drawn to an infectious recombinant RSV having a heterologous gene. Upon further consideration, the requirement to elect human or bovine polynucleotides from claim 6 is withdrawn. All other aspects of the restriction requirement are deemed proper and made final. Claims 1-207 are pending. Claims 68-95, 100-108 and 113-207 are withdrawn from consideration being drawn to non-elected inventions. Claims 1-67, 96-99 and 109-112 are examined on the merits.

Specification

2. The abstract of the disclosure is objected to because it exceeds 150 words.

Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 96-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a recombinant respiratory syncytial virus. Claim 96 is redundant, reciting that the virus of claim 1 is a virus. It is not clear how the virus of claim 1 can also be a subviral particle (claim 97).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-67, 96-99 and 109-112 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims read on embodiments of the claimed recombinant RSV wherein the virus comprises a RNA polymerase elongation protein. Thus, the claims as written encompass a generic class of recombinant RSV viruses, each of which may contain any RNA polymerase elongation factor. The specification does not provide adequate written description support for the full scope of these generic claims.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Also relevant to the discussion are the following excerpts from the case of In re Borkowski and Van Venrooy, 164 USPQ 642, (CCPA 1970). In describing the appropriate grounds for a claim rejection when the claim exceeds the scope of the disclosure, the court stated the following:

> *...a specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation.* (Excerpt from164 U.S.P.Q. at 645)

and;

> *... if the "enabling" disclosure of a specification is not commensurate in scope with the subject matter encompassed by a claim, that fact does not render the claim imprecise or indefinite or otherwise not in compliance with the second paragraph of §112; rather, the claim is based on an insufficient disclosure 4 (§112, first paragraph) and should be rejected on that ground. See In re Fuetterer, 50 CCPA 1453, 319 F.2d 259, 138 USPQ 217 (1963); In re Kamal, 55 CCPA 1409, 398 F.2d 867, 158 USPQ 320 (1968); and In re Wakefield, 164 USPQ (PA 8192), decided concurrently herewith. Thus, just as a claim which is of such breadth that it reads on subject matter disclosed in the prior art is rejected under §102 rather than under the second paragraph of §112, a claim which is of such breadth that it reads on subject matter as to which the specification is not "enabling" should be rejected under the first paragraph of §112.* (Excerpt from 164 U.S.P.Q. at 646).

Thus, when a claim covers a genus of inventions the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. However, a disclosure will also support the claims in the absence of examples if the description would enable one in the art to practice the invention without such guidance.

In the present case, the applicant has disclosed only a single example of a RNA polymerase elongation factor- the M2 ORF 1 protein of RSV. See e.g., pages 20, lines 4-6. Although the specification states that M2 ORF1 is only a preferred embodiment, neither the description nor the examples in the application provide any indication of what equivalents may

be. Without examples, or some identification of the M2 ORF1 structure that is necessary to its operation, one in the art wishing to practice the invention has no indication as to what other proteins may be used in the claimed virus. In view of the lack of description for any RNA polymerase elongation factor other than the M2 ORF1, the claims are rejected for exceeding the scope of descriptive support provided by the specification.

5. Claims 1-67, 96-99 and 109-112 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated infectious recombinant RSV wherein the virus comprises the M2 (ORF1) RNA polymerase elongation factor, does not reasonably provide enablement for viruses containing any RNA polymerase elongation factor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

A claim is commensurate in scope with the enablement when the applicant has provided sufficient disclosure to enable one skilled in the art to practice the claimed invention without undue experimentation. In re Wands, 8 USPQ2d 1400, 1404 (CAFC 1988). There must be a "reasonable correlation" between the scope of enablement and the scope of the claims. In re Fisher, 166 U.S.P.Q. 18, 24 (CCPA 1970). Such correlation requires "sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." See, In re

Vaeck, 20 U.S.P.Q.2d 1438, 1444 (CAFC 1991) No such guidance is provided in the present case.

The art relevant to the claimed invention (Collins *et al. PNAS USA* 92:11563-11567) indicates that the M2 ORF1 protein is one of the minimal proteins necessary for an infectious RSV (see abstract). Although the specification states that M2 ORF1 is only a preferred embodiment, it does not identify any characteristic or examples which one of ordinary skill in the art could use as guides to identify equivalents. Given the teachings of the specification and the disclosure of Collins, M2 ORF1 protein is necessary for an operative recombinant RSV. As the application has provided no examples or other indication as to what proteins fall within this subclass, other than the M2 ORF1 protein itself, the application has not provided an enabling disclosure corresponding to the full scope of the rejected claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-67, 96-99 and 109-112 are rejected under 35 U.S.C. 103(a) as being obvious over Collins (6,264,957) in view of Ball *et al* (*J. Virol.*, 1999, 73:4705-4712). The claims are drawn to an isolated, infectious recombinant respiratory syncytial virus comprising proteins N, P, L, a RNA polymerase elongation factor, and a partial or complete recombinant RSV genome or antigenome having one or more shifted RSV gene(s) or genome segment(s) within said

recombinant genome or antigenome. The genes or segments are shifted to a more promoter-proximal or promoter-distal position relative the genes' or segments' position within the wild type RSV genome or antigenome. Further limitations are drawn to displacement polynucleotides that can be deleted or inserted to shift genes. The displacement polynucleotides code for NS1, NS2, N, P, M, SH, M2-ORF1, M2-ORF2, L, F, G and leader, trailer and intergenic regions of RSV. The displacement polynucleotides can be from a bovine or human RSV. Claims are also drawn to an immunogenic composition comprising the recombinant RSV.

Collins teaches isolated, infectious recombinant RSV comprising proteins N, P, L, a RNA polymerase elongation factor (M2-ORF1), and a partial or complete recombinant RSV genome or antigenome. Modifications can be made to produce desired phenotypic changes, such as attenuation (abstract). Column 2, lines 57-67 and column 3 in its entirety, disclose various modifications that can be made to produce a recombinant RSV. Rearrangements, deletions, substitutions and insertions can be made to result in attenuation, temperature-sensitivity, cold-adaptations, small plaque size, etc. The foreign genes inserted can be from human, bovine and also different RSV subgroups. The recombinant RSV can be used in immunogenic compositions (abstract). *Collins is silent on the modification of shifting genes.*

However, Ball discloses rearrangements of P, M and G genes of Vesicular Stomatitis virus (VSV). These rearrangements resulted in viable, infectious viruses (abstract) having different phenotypes than the wild type.

It would have been obvious to make the rearrangements suggested by Ball to achieve desired phenotypes. One would have been motivated to make the modification of Ball in the RSV of Collins because Ball's VSV is a prototype of nonsegmented negative-strand RNA

viruses. Ball discloses that genes closer to the promoter site are transcribed at higher levels than those at more distal positions. One would have had a reasonable expectation of success that the rearrangements for VSV would have been successful in RSV because gene order between nonsegmented negative-strand RNA viruses is highly conserved (abstract of Ball). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time of the invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of copending Application No. 09/602,212. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claim is drawn to an infectious, recombinant RSV comprising a RSV genome having shifted genes. Claim 9 of the copending application is drawn

to an infectious, recombinant, chimeric (human and bovine) RSV comprising a RSV genome having shifted genes. Claim 9 is a species of claim 1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1, 2, 8 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-10 of copending Application No. 09/611,829 in view of Collins (6,264,957). The instant claim is drawn to an infectious, recombinant RSV comprising a RSV genome having shifted genes. The copending claims are drawn to an infectious, recombinant RSV comprising a RSV genome having shifted genes and partial or complete deletion of M2-ORF2. Collins discloses various modifications that can be made to produce a recombinant RSV, such as rearrangements, deletions, substitutions and insertions can be made to result in attenuation, temperature-sensitivity, cold-adaptations, small plaque size, etc. (column 2, lines 57-67 and column 3 in its entirety). It would have been obvious to incorporate the teachings of Collins into the copending claims. One would have been motivated to make deletions to achieve desired phenotypes because both Collins and the claims are drawn to similar systems of recombinant RSV production.

This is a provisional obviousness-type double patenting rejection.

Conclusion

9. No claim is allowed.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 6:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stacy S. Brown
March 21, 2003

HANKYEL T. PARK, PH.D
PRIMARY EXAMINER